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(72) Inventors:
• **Bartic, Carmen**
6600 Iasi (RO)
• **Poortmans, Jef**
3010 Leuven (BE)
• **Baert, Kris**
3001 Heverlee (BE)

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(71) Applicant: **INTERUNIVERSITAIR
MICRO-ELEKTRONICA CENTRUM VZW**
3001 Heverlee (BE)

(74) Representative: **Van Malderen, Joelle et al**
Office Van Malderen,
Place Reine Fabiola 6/1
1083 Bruxelles (BE)

(54) **A device for detecting an analyte in a sample based on organic materials**

(57) The present invention is related to a device for detecting an analyte in a sample comprising an active layer comprising at least a dielectric material, a source electrode, a drain electrode and a semiconducting substrate which acts as current pathway between source and drain. The conductance of said semiconducting layer can be influenced by the interaction of the active layer with the sample containing the analyte to detect. The device is fabricated such that properties like low price, disposability, reduced drift of the device and suitability for biomedical and pharmaceutical applications are obtained. To fulfil these requirements, the device described in this application will be based on organic containing materials.

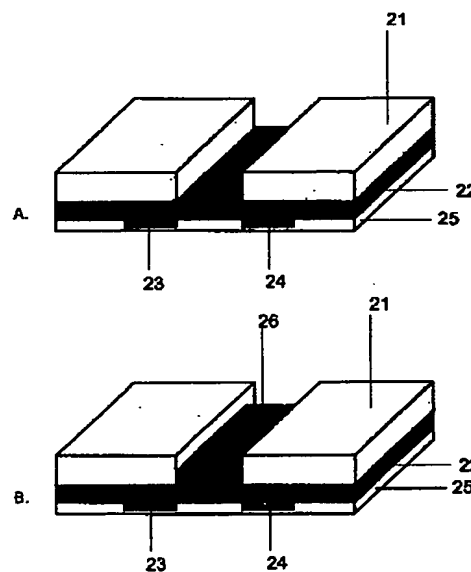


FIG. 2

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Description

Field of the Invention

[0001] The present invention is related to a device for detecting an analyte in a sample belonging to a class of devices known as chemically-sensitive field-effect transistors (CHEMFET's) which are of particular interest for biomedical and industrial applications.

Background of the Invention

[0002] There is considerable interest in methods for detection, measuring and monitoring chemical properties of a sample. A sample can be a solid, solution, gas, vapour or a mixture of those. The chemical properties of the sample are determined by the analyte present in the sample, the analyte can be e.g. an electrolyte, a biomolecule or a neutral molecule.

[0003] Chemical sensors belonging to a class of devices known as Chemically Sensitive Field-Effect Transistors (CHEMFET's) are of particular interest for biomedical and industrial applications. Chemically sensitive field-effect transistors measure chemical properties of the samples to which the device is exposed. In a CHEMFET, the changes at the surface of the gate dielectric are detected via the modulations of the electric field in the channel of a field-effect transistor. Such chemical changes can be induced by e.g. the presence of ions in aqueous solutions, but also by the interaction of an electroinactive organic compound with a biological-sensing element in contact with the gate of the field-effect transistor. In this way, the concentration of ions or organic biomolecules (e.g. glucose, cholesterol, etc) in aqueous solutions can be measured. One promising application of this type of device regards the monitoring of the cell metabolism for fundamental research or drug-characterisation studies.

[0004] Among CHEMFET devices, the ion-sensitive field-effect transistors are best known. The concept of ion-sensitive field-effect transistor (ISFET) has been introduced by P. Bergveld in 1970 [P. Bergveld, *IEEE Trans. Biomed. Eng.*, BME-17, 1970, pp. 70]. It was demonstrated that when the metal gate of an ordinary MOSFET is omitted and the dielectric layer is exposed to an electrolyte, the characteristics of the transistor are affected by the ionic activity of the electrolyte. The schematic drawing of a classic ISFET is shown in figure 1. The silicon substrate (1) of the device acts as current pathway between the source region (3) and the drain region (2). Both regions are contacted by metal electrodes (5). The dielectric layer (4) is covered with an ion-selective membrane (6) which is exposed to the solution (7). The device is encapsulated with an encapsulating material (9). Optionally, a reference electrode (8) can be present.

[0005] ISFET's have first been developed for pH and Na^+ activity detection in aqueous solutions (C. D. Fung,

P.W. Cheung and W. H. Ko, *IEEE Trans. EL Dev.*, Vol. ED-33, No.1, 1986, pp. 8-18). The cation-sensitivity of the device is determined by the ionisation and complexation of the surface hydroxyl groups on the gate dielectric surface. ISFET devices for Ca^{2+} , K^+ activity monitoring have also been fabricated. The sensitivity towards these ions is achieved by incorporating a sensitised plastic membrane (PVC) in contact with the gate dielectric. Therefore, these sensors detect changes in the charge of the membrane or in the transmembrane potential. Besides the use of CHEMFET devices for the determination of ions (ISFET), CHEMFET's have also been employed as enzyme-sensitive FET (ENFET's) for organic molecule detection or immuno-sensitive FET's (IMFET's) for immunochemicals (antigen, antibody) monitoring.

[0006] CHEMFET's exhibit important advantages over conventional chemically selective electrodes. Usually, CHEMFET's are fabricated with standard CMOS technology, which offers the advantages of miniaturisation and mass production. In the biomedical field, there is an especially important area for the application of miniaturised sensors. The sensor is mounted in the tip of indwelling catheters, through which their feasibility for monitoring blood electrolytes and parameters has been demonstrated.

[0007] The fabrication method offers the additional benefit of the fabrication of multi-ion sensors and integration in smart sensors and sensor arrays. A further advantage of the use of CHEMFET is the logarithmic response of the potential in function of the analyte concentration, this type of response is interesting if a broad concentration range is investigated. Since the response of a CHEMFET device is initiated by the field-effect, this response is very fast compared to the response of conventional chemically sensitive electrodes. Up to now, all CHEMFET devices are based on silicon or silicon based materials.

[0008] However, there are some problems that so far have hampered the commercial applications of these devices. The most important problem of the CHEMFET is the drift of the device. Drift is typically characterised by a relatively slow, monotonic temporal change in the threshold voltage of the FET. As a result, an incorrect estimation of the chemical properties (e.g. ion activity) of the sample will be determined. This problem is more pronounced for determination of e.g. physiological ion activities or concentrations, where a high accuracy is required (e.g. blood electrolytes monitoring). Therefore, the use of silicon-based CHEMFET's in this kind of applications is very reduced. A further limiting factor for the use of CHEMFET devices is the higher manufacturing cost of these devices. For medical application, one is mostly interested in throw-away devices, which implies very cheap devices. For medical and pharmaceutical applications, devices that can be integrated in plastic materials, are most suitable.

[0009] For silicon-based CHEMFET, the integration in

plastic material is not straightforward.

[0010] In the prior art, thin film transistors based on organic materials have been fabricated. Garnier (Garnier F., Hailaoui R., Yassar A., Srivastava P., Science, 1994, Vol. 265, p 1684) proposes the use of polymeric materials in a thin film transistor. The choice of polymeric materials is determined by the application of the device, i.e. as transistor.

[0011] Organic materials, and more especially polymeric materials, have already been used as sensitive parts in combination with a solid-state transducer (inorganic material) or as membranes for immobilisation of biomolecules (e.g. enzymes) for specific interactions (G. Harsányi, *Polymer Films in Sensor Applications - Technology, Materials, Devices and Their Characteristics*, TECHNOMIC Publishing Co. Inc. Lancaster-Basel, 1995, p 53-92 and p 149-155; G. Bidan, *Sensors and Actuators B*, Vol 6, 1992, pp. 45-56). In the electroconducting conjugated polymers-based (ECP-based) chemical sensors, there is a direct interaction between the ECP layer and the analyte to detect. The detection mechanism is based on the ion exchange between the ECP layer and the sample. Therefore, a doped ECP layer is needed. A major disadvantage is the required electrochemical deposition of the conducting layer, because this deposition technique is rather difficult to control, which results in the deposition of layers with a lower uniformity and reproducibility. Moreover, the electrochemical deposition of doped conjugated polymeric layers also implies a more complicated, multi-step process. Besides this, due to the electropolymerisation reactions, the electroconducting conjugated polymer layer is always p-doped, which means that only anions can be detected. Furthermore, the deposition process requires electrodes made of metallic material or glassy carbon.

Aims of the invention

[0012] The present invention aims to provide an improved device for detecting an analyte in a sample which combines the advantages of existing CHEMFET devices with advantageous properties such as low price, disposability, reduced drift of the device and suitability for biomedical and pharmaceutical applications.

Summary of the invention

[0013] In a first aspect of this invention, a device for detecting an analyte in a sample is disclosed comprising an active layer comprising at least a dielectric material, a source electrode, a drain electrode and a semiconducting layer for providing a current pathway between said source electrode and said drain electrode and wherein said semiconducting substrate consists of an organic containing semiconducting material and wherein said dielectric material of said active layer is substantially in contact with said semiconducting layer. The device is characterised in that said active layer is arranged

to contact said sample and to influence the conductance of said semiconducting layer when in contact with said sample containing said analyte to detect. Said Analyte, as used herein, shall be understood as any chemical molecule, atom or ion comprising but not limited to ions, neutral molecules and biomolecules like enzymes, immunochemicals, hormones and reducible gases. Sample, as used herein, shall be understood as a solid, solution, gas, vapour or a mixture of those comprising at least the analyte. For the purpose of this invention, detecting shall mean determining, identification, measuring of concentrations or activities, measuring a change of concentrations or activities of at least one analyte present in the sample.

[0014] In an embodiment of the invention, the active layer comprises a dielectric layer.

[0015] In an embodiment of this invention, the dielectric layer consists of a material with a dielectric constant higher than 3. In order to maximise the current flow between source and drain, the value of the dielectric constant must be as high as possible. Furthermore, a dielectric material with a high value of the dielectric constant will reduce the operational voltage of the device.

[0016] The chemically selective dielectric layer can be chosen such that the material of the dielectric layer is essentially inert to the sample. Inert shall, at least for the purpose of this application, mean that the capacitance of the dielectric layer without functionalisation remain practically constant. Thus, the problems related to the drift of the device can be eliminated. The drift phenomena is typically observed for silicon-based devices, since the silicon layer can be modified when exposed to the sample, resulting in a change of the capacitance of the dielectric layer. This results in slow, temporal change in the threshold voltage, which implies an incorrect estimation of the detection of the analyte.

[0017] In an embodiment of the invention, the active layer consists essentially of a dielectric layer. The dielectric layer is made of an active material arranged to selectively react with said analyte when said device is exposed to said sample containing said analyte. Depending on the application, the dielectric layer which is exposed to the sample can be modified in such a way that there is an interaction between the analyte and the modified dielectric material.

[0018] In an embodiment of the invention, the dielectric layer comprises an organic dielectric material. In a further embodiment of the invention, the dielectric layer comprises an inorganic containing material. The value of the dielectric capacitance is preferably as high as possible. The value of the dielectric constant, ϵ , of the dielectric material is higher than 3, and preferably higher than 5 and preferably higher than 10 and preferably higher than 100.

[0019] In a further embodiment of the invention, the active layer can further comprise a dielectric layer and a membrane layer. Said membrane layer is made of active material and is arranged to selectively react with

said analyte when the device is exposed to the sample containing the analyte. Preferably, the chemically sensitive membrane is a conjugated oligomer or a polymer.

[0020] In a further embodiment of the first aspect of the invention, the source and drain electrode comprise an organic containing material characterised in that said the surface resistance of the electrodes is lower than 100Ω/sq. The source and drain electrode can have an interdigitated configuration.

[0021] In a further embodiment of this invention, the device can additionally comprise an encapsulating layer to protect said current pathway between said source electrode and said drain electrode and a support layer wherein said encapsulating layer and support layer are made of organic containing material.

[0022] In a second aspect of this invention, a system for detecting an analyte in a sample is disclosed, comprising a device as described in the first aspect of this invention, and a reference field-effect transistor.

Short description of the drawings

[0023] Fig. 1 represents a description of an ion-sensitive field-effect transistor (ISFET) fabricated with CMOS technology (H. H. van den Vlekkert et. al., *Proc. 2nd Int. Meeting on Chemical Sensors, Bordeaux, France, 1986*, pp. 462.)

[0024] Figs. 2a and 2b represent the configuration of device according to the present invention.

[0025] Fig. 3 represents an interdigitated source-drain electrodes configuration.

[0026] Fig. 4 represents process flow and device configuration according to the preferred embodiment of the present invention.

Detailed description of the invention

[0027] In relation to the appended drawings the present invention is described in detail in the sequel. Several embodiments are disclosed. It is apparent however that a person skilled in the art can imagine several other equivalent embodiments or other ways of practicing the present invention, the spirit and scope thereof being limited only by the terms of the appended claims.

[0028] A device for detecting an analyte in a sample, based on organic materials is described. The device can be a chemically sensitive field-effective transistor (CHEMFET). Said device is a thin film transistor in which the gate electrode is missing and which comprises an active layer. Said active layer comprises at least a dielectric layer which is exposed to a sample comprising an analyte to be investigated directly or via a layer with a specific recognition function. Said device can be used for e.g. the detection and measuring of concentrations and activities of chemical species (analyte) present in the sample. Analyte, as used herein, shall be understood as any chemical molecule, atom or ion comprising but not limited to ions, neutral molecules and biomole-

cules like enzymes, immunochemicals, hormones and reducible gases. Sample, as used herein, shall be understood as a solution, solid, gas, vapour or a mixture of those comprising at least the analyte. For the purpose of this invention, detecting shall mean determining, identification, measuring of concentrations or activities, measuring a change of concentrations or activities of at least one analyte present in the sample. Particularly, said device can be used for the detection of analytes in samples in the biochemical and pharmaceutical field. Furthermore, said device can be used for the detection in samples containing specific analytes e.g. vapours, odour, gases.

[0029] In this invention, a device for detecting an analyte in a sample is disclosed, comprising a semiconductor layer, a source electrode, a drain electrode and an active layer. The active layer comprises at least a dielectric material. The semiconducting layer can be chosen such that it acts as current path between source and drain electrode. The electric field in the channel of the device is modified by the interaction of said active layer with an analyte in a sample. The choice of said semiconducting material can be further based on the conductivity of the material, the stability of the material, their availability, their compatibility with standard processing steps as used in the manufacturing of integrated circuits, their deposition characteristics and their cost price.

[0030] Said semiconducting layer can be adjacent to the active layer or can not be adjacent to the active layer.

[0031] The direct interaction of the semiconducting layer with the analyte is preferably negligible. In this invention, the semiconducting layer comprises an organic containing semiconducting material. The organic containing semiconducting material can be used in its neutral (undoped) state and can be a p-type semiconductor or an n-type semiconductor but preferably a p-type semiconductor. Said organic containing semiconducting material can be an organic polymer e.g. a conjugated polymers. Said conjugated polymer can be but is not limited to Polythiophene (PT), poly(p-phenylene) (PPP), poly(p-phenylene vinylene) (PPV), poly(2,5-thiophene vinylene) (PTV), polypyrrole (PPy) or C₆₀-buckminster fullerene. The organic containing semiconducting layer can also be a conducting oligomer layer wherein said oligomer layer can be but is not limited to α-hexylthiophene (α-6T), pentacene and oligophenylene vinylene.

[0032] The deposition of the organic containing semiconducting layer can be done by spin-coating, casting or evaporation of solution processible long-chain polymer or oligomer evaporation. Problems mentioned in the prior-art related to the deposition of electroconducting polymers are avoided by using the above mentioned deposition techniques.

[0033] In this invention, a device for detecting an analyte in a sample is disclosed, comprising a semiconductor layer, a source electrode, a drain electrode and